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BRINGING CLINICAL TRIALS TO LIFE

Arthritis Pain

Arthritis pain drug gets to market 18 months ahead of schedule

Highlights

- Synteract worked on a full-service study with an emerging biotech.
- It was responsible for enrollment, tracking product, capturing and keeping data clean.
- It met stringent timelines, ensured clean data, leading to timely product approval.

Introduction

In early 2014 Synteract took on a full-service study for an emerging biotech that was spun out of a large device company. **The orthobiologics company was working on non-surgical alternatives created to work with the body's biological processes to provide a natural lubricant into the joint that relieves mild to moderate pain, improves mobility, and helps the patient get back to their normal activities.**

The company came to Synteract to help it with a trial assessing efficacy with only 3 injections, rather than 5, of an already FDA-approved, non-surgical treatment for osteoarthritis. Although the company was familiar with Synteract from a rescue shut-down that Synteract had helped them with in France, this was the first study that this sponsor had conducted with Synteract from beginning to end and for this product.

Background

The solution of sodium hyaluronate used in visco-supplementation is injected directly into the knee joint to restore the cushioning and lubricating properties of synovial fluid (i.e., joint fluid), indicated for treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics like acetaminophen. Until this trial, it had been approved in the US only in a 5-injection cycle. The company wanted to prove that it could be effective in some patients with as few as 3 injections, to make it more attractive to insurance payers and patients alike. To make the claim officially and market it as such, the sponsor needed to prove the 3-injection product worked for at least six months and that it could be repeated if needed again later.

It was important for the sponsor to meet its timelines and corporate objectives to satisfy partner criteria and to prove itself as a young biotech. Meeting site selection and patient enrollment requirements were key – the initial goal established for enrollment was 9 months. The study was designed as a non-inferiority study – double blinded, with no placebo – patients were receiving either

the actual product or a comparator product that was already approved for 3 injections. Injections were to be given weekly for the first 3 weeks and follow-up was to be conducted for 26 weeks following the injection cycle.

Goals and Challenges

Interactions by Synteract with each site, including selection, motivation and communication were critical components of success. Synteract used a "swat team" of CRAs to conduct qualification visits and identify appropriate sites. According to the sponsor project manager, site selection was key.

"Synteract allowed for central IRB (institutional review board) approval for all sites – and there were 30 sites in the study – one IRB covered all of them. This cut down on administration and paperwork, and made it faster to get sites up and running quickly, which we needed to do to meet corporate objectives," said the sponsor's project manager.

Lots of patients have knee pain issues and many of the sites were quite excited about the product, so reaching patients was not too difficult once the protocol was established and sites selected. Under Synteract's guidance, the trial enrolled its first patient in March 2014 and last one in early August 2014, four months ahead of schedule. A total of 421 patients were enrolled for a target of 418.

The sponsor used a vendor to procure the drugs. Procuring both the comparator drug and the test drug, working within the timelines and constraints of the drug packaging vendor, turned out to be the biggest challenges. Unfortunately, the team was unable to purchase as much of either of the two drugs as they

wanted, resulting in 20% less than optimum – so they had to tightly manage the resources they had. Because it was a double blind study the team had to ensure that there was at least one of each product at each site at all times, on a 1:1 basis.

Tracking became critical, even on weekends. Synteract project team members constantly re-evaluated the inventory and were on the phone with sites continually reassessing who had product, who needed it and who was already enrolled vs. who looked to still be enrolling. A handful of sites that had lots of product but weren't enrolling as fast as others had to give some up – others that were enrolling faster were clamoring for product – and it took real diplomacy to calm everyone down and convince the ones with many portions to give some up! On top of all that, it was the very cold, icy winter of 2014 when the trial started and it was tough to ensure that the investigational product got shipped out from the Northeast in a manner that wouldn't strand it in the freezing cold. **Synteract team worked very closely with the vendor, the sponsor and the sites so they knew when to expect the drugs and how to use them with IWRS randomization so they would be set-up and ready to go as the patients came in for injections.** The team became quite good friends with FedEx, too!

"Many times when working through a CRO with sites, if the site's not happy, they'll try to manipulate it, even bad-mouth the CRO – but that never happened in this study – we received very positive feedback from the sites," says the sponsor. "This is important because the CRO represents the company and we want them to do so in a very positive manner. And it's especially challenging in a study like this where they were having to shift product back and forth. But they did such a great job of communication that the sites understood that they were close to enrolling completion and everyone tried to be cooperative. We received no complaints on any of the monitors either. It was a good group of CRAs."

During the follow-up and maintenance period, it was really important to keep the data clean and timely in order for the team to do the medical writing and hit the submission dates. The IDE had been submitted at the outset and the FDA did a study design review to assess the label change to be requested. After that there was minimal contact with the FDA until the full submission was completed.

There was lots of data to be captured – up to 9 visits apiece for 421 patients including 3 injections and 6 monthly follow-ups. Synteract put a WOMAC pain scale process in place so that patients could measure their own pain levels and report on them. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) is a widely used, proprietary set of standardized questionnaires used by health professionals to evaluate the condition of patients with osteoarthritis of the joints, and it includes pain, stiffness, and physical functioning. This was very helpful as it meant the patients didn't have to wait for a monitoring visit to report pain. A double measurement process using SynCapture EDC at Synteract validated the quality of the data.

The last patient follow-up visit occurred in Feb. 2015, then the database was cleaned and locked, the PMA supplement clinical doc was written and all data were submitted to the FDA. All this was completed between February and early December 2015. Synteract wrote the clinical study report and the clinical portion of the integrated summary of safety and efficacy.

Clean Data Leads to Fast Approval

Normally the FDA will do inspections at 10 percent of the investigator sites for quality assurance (which would have been 3 sites, in this case), and if there are any issues, the FDA will bump it up to 20 percent, meaning they could have required inspections of 6 sites. **In this case, after the FDA inspected the first two sites, which had immaculate data, they expressed no concerns at all. In fact, they were so confident in the quality of the data that they didn't even bother with a third. There were no negative findings.**

The product was approved in December, 2015 – even before the original projected date that had been the corporate objective to just complete the study! This improved the timeline by 1.5 years to get the product to market. Everyone was happy, with both the quality of the support and the resulting approval!

The project manager's final comment was this: "We would be very happy to work with Synteract again. They delivered a very responsive team with good communications. I've been doing this work for more than 25 years and I believe it very important that the CRO project team also 'owns' the project and doesn't just provide a service, but really cares about the quality of the trial and becomes part of the team. In this case, that's exactly what I got!"

About Synteract

Synteract is an innovative, full-service CRO supporting biopharma companies across all phases of drug development to help bring new medicines to market. Synteract has conducted 4,000 studies on six continents and in more than 60 countries, working with more than 26,000 investigative sites and 750,000 patients. It has contributed to more than 240 product approvals. Synteract offers a notable depth of expertise in oncology, general medicine, dermatology, and neuroscience indications, as well as rare and orphan, pediatric, and immunotherapy studies.

For more information on how we can support your clinical trial, please visit www.synteract.com/Services/Clinical-Operations or ContactUs@synteract.com.

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